Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 63, 68-76, 78-88, 94, 97-116, 118-123, 126 and 128-139 are pending in the application, with claim 63 being the sole independent claim. Claims 95, 117, 124, 125 and 127 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 74, 99, 105-107, 111-113, 121-123 and 133 have been withdrawn from consideration by the Examiner. New claims 134-139 are sought to be added. Support for the amendments can be found in paragraphs [0012-0018], [0175] and [0185-0188] of the published application, as well as in previous claim 95. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Request for Rejoinder

At page 2, the Examiner has withdrawn claim 133 as allegedly being directed to a non-elected invention. In accordance with MPEP § 821.04(a), a requirement for restriction should be withdrawn when a subcombination claim is allowable and any previously withdrawn claim that depends from or otherwise requires all the limitations of the subcombination should be rejoined. Here, claim 133 depends from claim 63. Applicants respectfully request that if the restriction requirement is made final, and allowability is determined of the group directed to a composition comprising a virus-like

particle of an RNA-bacteriophage with at least one first attachment site and ghrelin or ghrelin peptides as antigens or antigenic determinants with at least one second attachment site, then claim 133 directed to a process of producing the composition should be rejoined and examined for patentability. *See* M.P.E.P. § 821.04(a). Therefore, rejoinder and examination of claim 133 are respectfully requested.

Rejection under 35 U.S.C. § 103

At pages 3-5, the Examiner has rejected claims 63, 68-73, 75, 76, 78-88, 94, 95, 97, 98, 100-104, 108-110, 114-120, and 124-132 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Stockley *et al.* (U.S. Patent No. 6,159 728, hereinafter "Stockley") view of Deghengi *et al.* (US 2002/0187938728, hereinafter "Deghengi") and further in view of Kojima *et al.* (Nature, 1999, hereinafter "Kojima") and Maita *et al.* (Gen Pept Accession VCBPQB, 1971, hereinafter "Maita"). Applicants respectfully traverse this rejection.

As indicated in the specification, the presently claimed invention provides for compositions wherein ghrelin or ghrelin peptides are bound to virus-like-particles (VLPs) and subunits of VLPs, respectively, leading to highly ordered and repetitive conjugates representing potent immunogens for the induction of immune responses against ghrelin, in particular of high titers of anti-ghrelin antibodies (*see* paragraphs [0012]- [0018] of the published application, US 2004/0076645 A1).

Solely to advance prosecution, however, and not in acquiescence to the aforementioned rejections, claims 63 and 133 are now sought to be amended. The present claims, thus recite compositions comprising a virus-like particle of an RNA-

bacteriophage with at least one first attachment site and ghrelin or ghrelin peptides as antigens or antigenic determinants with at least one second attachment site, wherein *said first attachment site is a lysine residue of said virus-like particle, and wherein said second attachment is a cysteine residue; and wherein said composition induces an immune response against ghrelin, when administered to a mammal*.

In contrast, the references cited by the Examiner, viewed alone or in combination, neither disclose nor suggest all of the elements of the previously pending claims nor of the present claims. Thus, the Examiner has not satisfied the burden of establishing a *prima facie* case of obviousness based upon the cited art. *See In re Piasecki*, 745 F.2d 1468, 1471-72 (Fed. Cir. 1984). The factors to be considered under 35 U.S.C. § 103(a) are the scope and content of the prior art; the differences between the prior art and the claims at issue; and the level of ordinary skill in the pertinent art. *See Graham v. John Deere*, 86 S.Ct. 684 (1966) and MPEP §2141. This analysis has been the standard for 40 years, and remains the law today. *See KSR International Co v. Teleflex Inc.*, 127 S.Ct. 1727 (2007). The critical role of the Office personnel as fact finders when resolving *Graham* inquiries has been emphasized by the Office within its published Examination Guidelines. *See* "Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in KSR International v. Teleflex Inc"., *Fed. Reg.* 72:57526- 57535 (October 10, 2007), hereinafter "Examination Guidelines." Establishment of a *prima facie* case of obviousness requires that the Examiner factually show that the references in combination disclose all of the elements of the claims in its proper function, as well as provide a reasoned articulation that the combination of

elements would have been known to produce a predictable result. In the present case, this burden has not been met.

In making this rejection, the Examiner asserted that:

> Stockley teaches pharmaceutical compositions comprising virus like particles of an RNA bacteriophage, particularly the Qβ bacteriophage as an antigen delivery system (see the entire document, particularly claims 1-12). Stockley teaches the non-peptide covalent coupling between the RNA bacteriophage and *the antigen of interest* (see column 3, lines 22-44, column 12, lines 8-29 and claim 8).

Office Action at pages 3-4 (Emphasis added). Furthermore, the Examiner asserted that:

> Thus it would have been *prima facie* obvious to the person of ordinary skill in the art to provide Stockley's pharmaceutical composition comprising the RNA Qβ bacteriophage *covalently coupled* to Deghenghi's and/or Kojima's ghrelin peptide *as an antigenic determinant*, because *Stockley teach that RNA Qβ bacteriophages serve as efficient delivery systems for foreign antigens* and because Deghenghi teaches administration of ghrelin peptides for therapeutic purposes.

Office Action at pages 5 (Emphasis added).

Applicants respectfully disagree with all of these assertions and traverse the rejections.

Contrary to the Examiner's assertions, Stockley relates to "a protein-based delivery system and is particularly directed to the delivery of *encapsidated foreign moieties*, especially to targeted sites in the human or animal body" (*see* Stockley column 1, lines 4-7, emphasis added).

More specifically, Stockley relates to "a delivery system comprising a capsid formed from a coat protein of a bacteriophage of MS-2 or related phage and *a foreign moiety enclosed in the capsid* (*see* Stockley, Claim1 and column 1, lines 53-65, emphasis added). Furthermore, within the paragraphs cited by the Examiner, Stockley describes then a preferred form of the delivery system, in which "*a targeting moiety* is

directly attached to the coat protein or linked to the coat protein through a spacer moiety (*see* Stockley, Claim 8 and column 2, lines 10-15, emphasis added).

However, in contrast to the Examiner's assertion that "Stockley teaches the non-peptide covalent coupling between the RNA bacteriophage and *the antigen of interest*, Stockley only and explicitly refers to "*a targeting moiety* directly attached or linked to the coat protein." This becomes even more apparent, when referring to column 3, lines 22-32, a paragraph explicitly mentioned by the Examiner:

> The cysteine residue, or alternative modification site, can be further linked to *a targeting moiety* with or without interposition of a further spacer moiety. An example of such a targeting moiety is a galactose residue *which can be used to direct the capsids to interact with specific cell surface receptors and thus carry the foreign moiety within the capsids to and/or into specific cells*. Other possible targeting moieties are other cell surface receptor ligands or monoclonal antibodies. Suitable receptors for the targeting moieties are the asialoglycoprotein receptor and the receptor for melanocyte stimulating hormone.

(Emphasis added).

Thus, Applicants respectfully disagree with the assertion that "Stockley teaches a non-peptide covalent coupling between the RNA bacteriophage and *an antigen of interest*." To the contrary, the purpose and function of the targeting moiety is to *deliver* Stockley's foreign moiety *to the sites in the body where the foreign moiety's activity is required* (*see* Stockley column 1, lines 8-12, emphasis added). Therefore, the induction of immune responses against the targeting moiety, in particular high titers of antibodies specific for this targeting moiety, would defeat the purpose intended by Stockley, namely "to deliver the foreign moieties to the site where they are to act" (*see* Stockley column 1, lines 8-12). Instead, if an immune response against the targeting moiety of Stockley was induced, the complexes of Stockley would never work for their intended purpose, since

they would be cleared by the immune system before they could deliver the foreign encapsidated moiety to the desired site within the body.

Furthermore, Stockley does *not* disclose or suggest compositions comprising a virus-like particle of an RNA-bacteriophage with at least one first attachment site and ghrelin or ghrelin peptides as antigens or antigenic determinants with at least one second attachment site, wherein *said first attachment site is a lysine residue of said virus-like particle and wherein said second attachment is a cysteine residue*, as is required by the present claims.

Accordingly, Stockley is seriously deficient as a primary reference upon which to attempt to base a *prima facie* case of obviousness.

Moreover, neither Deghenghi nor Kojima or Maita disclose compositions comprising a virus-like particle of an RNA-bacteriophage with at least one first attachment site and ghrelin or ghrelin peptides as antigens or antigenic determinants with at least one second attachment site, wherein said first attachment site is a lysine residue of said virus-like particle and wherein said second attachment is a cysteine residue, as, *inter alia*, required by the present claims.

Therefore, neither Deghenghi nor Kojima or Maita supplement the deficiencies of Stockley, and the references cannot be properly combined in an attempt to make out a *prima facie* case of obviousness of the formerly pending and present claims.

In view of the foregoing remarks, Applicants respectfully assert that the present claims would not have been obvious over Stockley and Deghenghi, Kojima and Maita, alone or in combination. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) over these reference are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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